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=> file uspat
FILE 'USPAT' ENTERED AT 14:49:08 ON 07 JAN 97

  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *              W E L C O M E   T O   T H E                    *
  *         U. S.   P A T E N T   T E X T   F I L E             *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> s acetic acid(5a)lyophil?(10a)peptide
        115920 ACETIC
        391843 ACID
        102715 ACETIC ACID
                  (ACETIC(W)ACID)
         19118 LYOPHIL?
         17043 PEPTIDE
L4         288 ACETIC ACID(5A)LYOPHIL?(10A)PEPTIDE

=> s l4 and py<1994
       1758474 PY<1994
L5         192 L4 AND PY<1994

=> d kwic 1-10

US PAT NO:     5,273,960 [IMAGE AVAILABLE]            L5: 1 of 192
DATE ISSUED:   **Dec. 28, 1993**

SUMMARY:

BSUM(10)

 In . . . Lys Asp Val were isolated in amorphous state. Both amorphous
and air dried substances contain 70 to 85% of a **peptide**, the rest
consists of water, **acetic** **acid** and ethanol. **Lyophilized**
substances generally contain 15% of **acetic** **acid**. Both the water
and the acetic acid content significantly depends on the technological
circumstances (starting substance concentration, lyophilization program,
drying. . .
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US PAT NO: 5,268,455 [IMAGE AVAILABLE] L5: 2 of 192
DATE ISSUED: **Dec. 7, 1993**

DETDESC:

DETD(110)

Crude **peptide** was removed from the resin with 10% aqueous **acetic** **acid** and **lyophilized**. The **peptide** was purified via HPLC on Vydac C18 using a water-acetonitrile/0.1% trifluoroacetic acid (TFA) elution system. The polypeptide was lyophilized and. . .

US PAT NO: 5,268,360 [IMAGE AVAILABLE] L5: 3 of 192
DATE ISSUED: **Dec. 7, 1993**

DETDESC:

DETD(99)

Subsequently, hydrogen fluoride was distilled off under reduced pressure and the residue was extracted with 30% **acetic** **acid** and **lyophilized** to afford 150 mg of a crude **peptide**. The crude **peptide** was purified by reversed-phase chromatography (RPC) using an octadecyl silane (ODS) column (Cosmosil 5 C.sub.18 -AR, Nacalai Tesque Inc.) to. . .

US PAT NO: 5,268,267 [IMAGE AVAILABLE] L5: 4 of 192
DATE ISSUED: **Dec. 7, 1993**

DETDESC:

DETD(47)

Amino Acid Analysis--The acyl-**peptide** hydrolase was dialyzed extensively against 0.1M **acetic** **acid**, **lyophilized**, and hydrolyzed at 110.degree. C. for 24 hr and 48 hr in 6M HCl containing 0.1% phenol. The amino acid. . .

US PAT NO: 5,268,164 [IMAGE AVAILABLE] L5: 5 of 192
DATE ISSUED: **Dec. 7, 1993**

DETDESC:

DETD(43)

The . . . at 0.degree. C. The HF was removed in vacuo and the crude resin/peptide was washed with ether three times. The **peptide** was extracted with 10% **acetic** **acid** and **lyophilized** to yield a crude **peptide**.

US PAT NO: 5,258,368 [IMAGE AVAILABLE] L5: 6 of 192
DATE ISSUED: **Nov. 2, 1993**

DETDESC:

DETD(229)

The . . . diethyl ether. The peptide/resin mixture was washed twice with diethyl ether, twice with chloroform, and twice with diethyl ether. The **peptide** was extracted with 2.0M **acetic** **acid** and **lyophilized**, to give the unoxidized dihydro **peptide**.

US PAT NO: 5,252,718 [IMAGE AVAILABLE] L5: 7 of 192
DATE ISSUED: **Oct. 12, 1993**

DETDESC:

DETD(6)

After . . . of the HF under high vacuum, the resin-peptide remainder is washed alternately with dry diethyl ether and chloroform, and the **peptide** is then extracted with degassed 2N aqueous **acetic** **acid**. **Lyophilization** of the **acetic** **acid** extract provides a white fluffy material.

US PAT NO: 5,252,713 [IMAGE AVAILABLE] L5: 8 of 192
DATE ISSUED: **Oct. 12, 1993**

SUMMARY:

BSUM(44)

Peptide . . . protecting groups are removed using the Tam-Merrifield low-high HF procedure (Tam et al., J. Am. Chem. Soc. 105:6442-55, 1983). The **peptide** can be extracted with 20% **acetic** **acid**, **lyophilized**, and purified by reversed-phase HPLC on a Vydac C-4 Analytical Column using a linear gradient of 100% water to 100%. . .

US PAT NO: 5,252,705 [IMAGE AVAILABLE] L5: 9 of 192
DATE ISSUED: **Oct. 12, 1993**

DETDESC:

DETD(9)

The . . . hour. After evaporation of the reaction mixure under reduced pressure, the residue was washed with ethyl acetate, extracted with 1M **acetic** **acid**, and **lyophilized** to obtain crude **peptide**. The crude **peptide** was applied to reverse phase high pressure chromatography, and eluted with linear gradient of water-acetonitrile containing 0.1% trifluoroacetic acid. After. . .

US PAT NO: 5,247,067 [IMAGE AVAILABLE] L5: 10 of 192
DATE ISSUED: **Sep. 21, 1993**

DETDESC:

DETD(25)

Specifically, . . . was thoroughly washed with diethyl ether and dichloromethane on a glass filter. The washed residue was extracted with 2N aqueous **acetic** **acid**, and the extract was **lyophilized** to yield 200 mg of a crude **peptide**. The crude product thus obtained was

subjected to preparative reversed phase high performance liquid chromatography [column: packed with octadecylated silica. . .

=>
=>
=> d kwic 100-120

US PAT NO: 4,716,147 [IMAGE AVAILABLE] L5: 100 of 192
DATE ISSUED: **Dec. 29, 1987**

DETDESC:

DETD(6)
The . . . resin using HF/anisole (9:1, v/v) and 2-mercaptopyridine (150 mg/g of peptide-resin) at 0 degrees for 1 hour. The crude free **peptide** was extracted with 30% **acetic** **acid**/water and **lyophilized**.

DETDESC:

DETD(8)

The . . . (pH 7.8) at a concentration of 0.1 mg/ml for 20 hours. The solution was then acidified to pH 2 with **acetic** **acid** and **lyophilized**. The cyclized **peptide** was purified using the conditions described above and its purity was analyzed by HPLC on a Vydac C-18 reversed phase. . .

US PAT NO: 4,711,877 [IMAGE AVAILABLE] L5: 101 of 192
DATE ISSUED: **Dec. 8, 1987**

DETDESC:

DETD(28)

The . . . pyridine-acetate buffer (30:4:66, pyridine/glacial acetic acid/water). The pyridine acetate solution is then removed by distillation in vacuo. The residue was **lyophilized** from 5% **acetic** **acid** to give the titled **peptide** which is purified as described above.

DETDESC:

DETD(30)

The . . . column is eluted with pyridine-acetate buffer (30:4:66), pyridine/HOAc/H.sub.2 O) The pyridine acetate solution is removed in vacuo. The residue is **lyophilized** from 10% **acetic** **acid** to give the crude titled **peptide** which is purified as above.

DETDESC:

DETD(38)

Product containing fractions (TLC) are combined and concentrated. The residue is dissolved in conc. **acetic** **acid**, diluted with water and **lyophilized** to yield the acid **peptide**.

US PAT NO: 4,709,012 [IMAGE AVAILABLE] L5: 102 of 192
DATE ISSUED: **Nov. 24, 1987**

DETDESC:

DETD(7)

The . . . was removed from the resin and deprotected using liquid HF/anisole (9:1, v/v) at 0 degrees for one hour. The crude **peptide** was extracted from the resin with 50% aqueous **acetic** **acid** and **lyophilized**.

US PAT NO: 4,704,451 [IMAGE AVAILABLE] L5: 103 of 192
DATE ISSUED: **Nov. 3, 1987**

DETDESC:

DETD(12)

Following washing of the resin with dry ethyl ether, the crude **peptide** was extracted in 10% **acetic** **acid** and **lyophilized**. The **peptide** was simultaneously desalted and definitively purified on a DEAE-Sephacel column and eluted with linear salt gradients developed in varigrad device. . .

US PAT NO: 4,704,380 [IMAGE AVAILABLE] L5: 104 of 192
DATE ISSUED: **Nov. 3, 1987**

DETDESC:

DETD(12)

Following washing of the resin with dry ethyl ether, the crude **peptide** was extracted in 10% **acetic** **acid** and **lyophilized**. The **peptide** was simultaneously desalted and definitively purified on a DEAE-Sephacel column and eluted with linear salt gradients developed in a varigrad. . .

US PAT NO: 4,701,499 [IMAGE AVAILABLE] L5: 105 of 192
DATE ISSUED: **Oct. 20, 1987**

SUMMARY:

BSUM(17)

As . . . is preferably added to the peptidoresin prior to treatment with HF. After removal of HF under vacuum, the cleaved, deprotected **peptide** is conveniently treated with ether, decanted, taken-up in dilute **acetic** **acid**, and **lyophilized**.

US PAT NO: 4,697,002 [IMAGE AVAILABLE] L5: 106 of 192
DATE ISSUED: **Sep. 29, 1987**

SUMMARY:

BSUM(15)

Cleavage . . . fluoride in the presence of anisole (Yamashiro, D. and Li, C. H. (1978) J. Am. Chem. Soc. 100, 5174-5179). Crude **peptide** is removed from the resin by washing with 10% aqueous **acetic** **acid**. After **lyophilization**, the residue may be treated with dithiothreitol (Cleland, W. W. (1964) Biochemistry 3, 480-482) in sodium phosphate buffer at pH. . .

US PAT NO: 4,693,993 [IMAGE AVAILABLE] L5: 107 of 192
DATE ISSUED: **Sep. 15, 1987**

DETDESC:

DETD(22)

A . . . portions of ethyl ether (Et.sub.2 O) and the peptide extracted into glacial acetic acid using three 6 ml extractions. The **acetic** **acid** solution was **lyophilized** to give 185 mg of crude deprotected **peptide**.

DETDESC:

DETD(23)

The . . . as determined by the quantitative Sakaguchi reagent, was collected, the solvent evaporated under reduced pressure, the residue dissolved in glacial **acetic** **acid** (AcOH) and **lyophilized** to give 140 mg of **peptide** with a partition coefficient (k) from the CCD of 5.7. Repeating the countercurrent distribution in the solvent system nBuOH:AcOH:H2O(4:1:5) gave,. . .

US PAT NO: 4,689,396 [IMAGE AVAILABLE] L5: 108 of 192
DATE ISSUED: **Aug. 25, 1987**

PARENT-CASE:

This . . .

preferably added to the peptide prior to treatment with HF. After the removal of HF, under vacuum, the cleaved, deprotected **peptide** is conveniently treated with ether, decanted, taken-up in dilute **acetic** **acid** and **lyophilized**.

Purification of the peptide is effected by ion exchange chromatography on a CMC column, followed by partition chromatography using. . .

DETDESC:

DETD(10)

After . . . as a scavenger prior to HF treatment. After the removal of HF under vacuum, the resin is extracted with 50% **acetic** **acid**, and the washings are **lyophilized** to provide a crude **peptide** powder.

US PAT NO: 4,687,839 [IMAGE AVAILABLE] L5: 109 of 192
DATE ISSUED: **Aug. 18, 1987**

SUMMARY:

BSUM(16)

Cleavage . . . fluoride in the presence of anisole (Yamashiro, D. and Li, C. H. (1978) J. Am. Chem. Soc. 100, 5174-5179). Crude **peptide** is removed from the resin by washing with 10% aqueous **acetic** **acid**. After **lyophilization**, the residue may be treated with dithiothreitol (Cleland, W. W. (1964) Biochemistry 3, 480-482) in sodium phosphate buffer at pH. . .

US PAT NO: 4,687,758 [IMAGE AVAILABLE] L5: 110 of 192
DATE ISSUED: **Aug. 18, 1987**

DETDESC:

DETD(29)

Pmp(4-MeBzl)-Ile-Phe-Abu-Asn-Cys(4-MeBzl)-MeArg-(Tos)-Gly-BHA-Resin, . . . eluted with pyridine-acetate buffer (30:4:66, pyridine/acetic acid/water). The pyridine acetate solution is removed by distillation in vacuo. The residue is **lyophilized** from 1% **acetic** **acid** to give the titled **peptide**. Purification is carried out as in Example 3 below.

US PAT NO: 4,684,622 [IMAGE AVAILABLE] L5: 111 of 192
DATE ISSUED: **Aug. 4, 1987**

DETDESC:

DETD(19)

The . . . pyridine-acetate buffer (30:4:66, pyridine/glacial acetic acid/water). The pyridine acetate solution was then removed by distillation in vacuo. The residue was **lyophilized** from 5% **acetic** **acid** to give 610 mg (60%) of crude titled **peptide**.

DETDESC:

DETD(40)

The . . . column was eluted with pyridine-acetate buffer (30:4:66), pyr/HOAc/H.sub.2 O). The pyridine acetate solution was removed in vacuo. The residue was **lyophilized** from B 10% **acetic** **acid** to give 525 mg (75%) of crude titled **peptide**.

DETDESC:

DETD(60)

The . . . column was eluted with pyridine-acetate buffer (30:4:6, pyr/HOAc/H.sub.2 O). The pyridine-acetate solution was removed in vacuo, and the residue was **lyophilized** from 10% **acetic** **acid** to give 450 mg (83.85%) of the crude titled **peptide**.

DETDESC:

DETD(129)

Product containing fractions (TLC) are combined and concentrated. The residue is dissolved in conc. **acetic** **acid**, diluted with water and **lyophilized** to yield the acid **peptide**. The Cys(OH) or Z(OH) intermediates are used, without further purification, for the synthesis of the end product peptides.

US PAT NO: 4,677,193 [IMAGE AVAILABLE] L5: 112 of 192
DATE ISSUED: **Jun. 30, 1987**

SUMMARY:

BSUM(33)

The . . . Solid-Phase Peptide Synthesis, G. Barany & R. Merrifield, p. 192-197. After the removal of HF under vacuum, the cleaved, deprotected **peptide** is conveniently treated with ether, decanted, taken-up in dilute **acetic** **acid** and **lyophilized**. At this point, the **peptide** can, if desired, be converted to its nontoxic salt, as by treatment, for example, with 1 N acetic acid.

DETDESC:

DETD(10)

After . . . treatment to produce the mixed alkyl ketone. After the removal of HF under vacuum, the resin is extracted with 50% **acetic** **acid**, and the washings are **lyophilized** to provide a crude **peptide** powder.

DETDESC:

DETD(34)

After . . . most cases to act as a scavenger. After the removal of HF under vacuum, the resin is extracted with 50% **acetic** **acid**, and the washings are **lyophilized** to provide a crude **peptide** powder.

DETDESC:

DETD(39)

The . . . fumarate, gluconate, tannate, maleate, acetate, citrate, benzoate, succinate, alginate, malate, ascorbate, tartrate and the like. An aqueous solution of the **peptide** is repeatedly treated, for example, with 1N **acetic** **acid** and then **lyophilized** to yield the acetic acid salt thereof. If the active ingredient is to be administered in tablet form, the tablet. . .

US PAT NO: 4,665,157 [IMAGE AVAILABLE] L5: 113 of 192
DATE ISSUED: **May 12, 1987**

SUMMARY:

BSUM(23)

The . . . compound of interest elutes at the end of the 0 to 0.3M pyridine gradient. The fractions which include the desired **peptide** were concentrated in vacuo, redissolved in 50% **acetic** **acid** and **lyophilized**. This ion-exchange chromatography step was repeated in the same manner as described above on the desired isolated fraction. Final purification. . .

US PAT NO: 4,663,309 [IMAGE AVAILABLE] L5: 114 of 192
DATE ISSUED: **May 5, 1987**

DETDESC:

DETD(4)

MCT-I . . . treatment with anhydrous liquid hydrofluoric acid in the presence of anisole (7:1, v/v) at 0.degree. C. for 45 min. Crude **peptide** was removed from the resin by washing with 10% **acetic** **acid**. The residue remaining after **lyophilization** was treated with excess dithiothreitol in 0.05M sodium phosphate buffer at pH 7.0. The intramolecular disulfide bond between cysteine residues. . .

US PAT NO: 4,661,472 [IMAGE AVAILABLE] L5: 115 of 192
DATE ISSUED: **Apr. 28, 1987**

DETDESC:

DETD(10)

After . . . as a scavenger prior to HF treatment. After the removal of HF under vacuum, the resin is extracted with 50% **acetic** **acid**, and the washings are **lyophilized** to provide a crude **peptide** powder.

DETDESC:

DETD(52)

The . . . tannate, maleate, acetate, citrate, benzoate, succinate, alginate, malate, ascorbate, tartrate and the like. For example, an aqueous solution of the **peptide** can be repeatedly treated with 1N **acetic** **acid** and then **lyophilized** to yield the **acetic** **acid** salt thereof. If the active ingredient is to be administered in tablet form, the tablet may contain a pharmaceuticallyacceptable diluent. . .

US PAT NO: 4,658,014 [IMAGE AVAILABLE] L5: 116 of 192
DATE ISSUED: **Apr. 14, 1987**

SUMMARY:

BSUM(23)

Cleavage . . . hydrogen fluoride in the presence of anisole (Yamashiro, D and Li, C. H. (1978) J. Am. Chem. Soc. 100,5174-5179). Crude **peptide** is removed from the resin by washing with 10% aqueous **acetic** **acid** and is then **lyophilized**. When the intramolecular

disulfide bond in the **peptide** is present, the residue may be treated with dithiothreitol and the disulfide between residues 1 and 7 can be formed. . .

US PAT NO: 4,652,627 [IMAGE AVAILABLE] L5: 117 of 192
DATE ISSUED: **Mar. 24, 1987**

DETDESC:

DETD(40)

Cleavage . . . fluoride in the presence of anisole (Yamashiro, D. and Li, C. H. (1978) J. Am. Chem. Soc. 100, 5174-5179). Crude **peptide** is removed from the resin by washing with 10% aqueous **acetic** **acid**. After **lyophilization**, the residue may be treated with dithiothreitol (Cleland, W. W. (1964) Biochemistry 3, 480-482) in sodium phosphate buffer at pH. . .

US PAT NO: 4,652,550 [IMAGE AVAILABLE] L5: 118 of 192
DATE ISSUED: **Mar. 24, 1987**

SUMMARY:

BSUM(31)

The . . . preferably added to the peptide prior to treatment with HF. After the removal of HF, under vacuum, the cleaved, deprotected **peptide** is conveniently treated with ether, decanted, taken-up in dilute **acetic** **acid** and **lyophilized**.

DETDESC:

DETD(13)

After . . . as a scavenger prior to HF treatment. After the removal of HF under vacuum, the resin is extracted with 50% **acetic** **acid**, and the washings are **lyophilized** to provide a crude **peptide** powder.

DETDESC:

DETD(31)

The . . . tannate, maleate, acetate, citrate, benzoate, succinate, alginate, malate, ascorbate, tartrate and the like. For example, an aqueous solution of the **peptide** can be repeatedly treated with 1N **acetic** **acid** and then **lyophilized** to yield the **acetic** **acid** salt thereof. If the active ingredient is to be administered in tablet form, the tablet may contain a pharmaceutically-acceptable diluent. . .

US PAT NO: 4,644,054 [IMAGE AVAILABLE] L5: 119 of 192
DATE ISSUED: **Feb. 17, 1987**

SUMMARY:

BSUM(38)

Cleavage . . . fluoride in the presence of anisole (Yamashiro, D. and Li, C. H. (1978) J. Am. Chem. Soc. 100, 5174-5179). Crude **peptide** is removed from the resin by washing with 10% aqueous **acetic** **acid**. After **lyophilization**, the residue may be treated with dithiothreitol (Cleland, W. W. (1964) Biochemistry 3, 480-482) in sodium phosphate buffer at pH. . .

US PAT NO: 4,643,988 [IMAGE AVAILABLE] L5: 120 of 192
DATE ISSUED: **Feb. 17, 1987**

DETDESC:

DETD(23)

Release . . . for 15 h. The reaction mixture was diluted with ether (500 ml) and filtered. The residue was washed with 50% **acetic** **acid**, diluted with water and **lyophilized** to obtain 230 mg of the **peptide**. This was then treated with 0.1M hydroxylamine hydrochloride solution (pH 9.5 100 ml) for 15 h. The pH was adjusted. . .

=> log h
SESSION WILL BE HELD FOR 30 MINUTES

U.S. Patent & Trademark Office SESSION SUSPENDED AT 15:21:24 ON 07 JAN 199